II. AMENDMENT OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the Application.

LISTING OF CLAIMS

Claim 1. (Original)A solid oral controlled-release dosage form suitable for 24 hour dosing in a human patient comprising a pharmaceutically acceptable matrix comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material; said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85; and said dosage form providing a therapeutic effect for at least about 24 hours.

Claim 2. (Original)The dosage form of claim 1, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 3. (Original)The dosage form of claim 1, wherein said matrix is a plurality of multiparticulate matrices.

Claim 4. (Original)The dosage form of claim 3, wherein said multiparticulates are compressed into a tablet.

Claim 5. (Original)The dosage form of claim 3, wherein said multiparticulates are disposed in a pharmaceutically acceptable capsule.

Claim 6. (Original)The dosage form of claim 1 which provides a C_{24}/C_{max} ratio of 0.60 to 0.70.

Claim 7. (Original)The dosage form of claim 1 which provides a dissolution release rate in-vitro of the hydrocodone when measured by the USP Basket method at 100rpm in

700 ml aqueous buffer at a pH of 1.2 at 37° C is at least 10% to about 45% by weight hydrocodone or salt thereof released at 1 hour.

Claim 8. (Original)The dosage form of claim 1, which provides a dissolution release rate in-vitro of the hydrocodone or salt thereof when measured by the USP Basket Method at 100 rpm in 700 ml Simulated Gastric Fluid (SGF) at 37° C for 1 hour and thereafter switching to 900 ml with Phosphate Buffer to a pH of 7.5 at 37 ° \C, of at least 20% by weight hydrocodone or salt thereof released at 4 hrs, from about 20% to about 65% by weight hydrocodone or salt thereof released at 8 hrs, from about 45% to about 85% by weight hydrocodone or salt thereof released at 12 hrs, and at least 80% by weight hydrocodone or salt thereof released at 24 hours.

Claim 9. (Original)The dosage form of claim 1, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 10. (Original)The dosage form of claim 1, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 11. (Original)The dosage form of claim 1, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 12. (Original)The dosage form of claim 1, wherein said administration is first administration.

Claim 13. (Original)The dosage form of claim 1, wherein said administration is steady state administration.

Claim 14. (Original)The dosage form of claim 1, wherein said ratio is provided to a population of patients.

Claim 15. (Original)A solid oral controlled-release dosage form suitable for 24 hour dosing in a human patient comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material, said dosage form after oral administration, providing a rate of absorption during the time period from T_{max} to about 24 hours after oral administration of the dosage form which is from about 45% to about 85% of the rate of elimination during the same time period, said dosage form providing a therapeutic effect for at least about 24 hours.

Claim 16. (Original)A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form comprising a pharmaceutically acceptable matrix comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material, said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85 and a therapeutic effect for at least about 24 hours.

Claim 17. (Original)A process for the preparation of a solid oral controlled-release dosage form, comprising incorporating an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof into a controlled release material, said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85 and a therapeutic effect for at least about 24 hours.

Claim 18. (Currently Amended) A solid oral controlled-release dosage form suitable for 24 hour dosing in a human patient comprising a plurality of pharmaceutically acceptable beads coated with an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and overcoated with a pH-independent hydrophobic material <u>comprising an acrylic polymer</u>, said dosage form providing an in-vitro release rate, of hydrocodone or a pharmaceutically acceptable salt thereof, when measured by the USP Basket Method at 100 rpm in 900 ml aqueous buffer at a pH of

between 1.6 and 7.2 at 37° C of from 0% to about 35% at 1 hour, from about 10% to about 70% at 4 hours, from about 20% to about 75% at 8 hours, from about 30% to about 80% at 12 hours, from about 40% to about 90% at 18 hours, and greater than about 60% at 24 hours; the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer, is no greater than 10%; said dosage form providing a C24/C_{max} ratio of 0.55 to about 0.85; and a therapeutic effect for at least 24 hours, after oral administration to a human patient.

Claim 19. (Original)The dosage form of claim 18, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 20. (Original)The dosage form of claim 18, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 21. (Original)The dosage form of claim 18, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 22. (Original)The dosage form of claim 18, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 23. (Original)The dosage form of claim 18, wherein said administration is first administration.

Claim 24. (Original)The dosage form of claim 18, wherein said administration is steady state administration.

Claim 25. (Original)The dosage form of claim 18, wherein said ratio is provided to a population of patients.

Claim 26. (Original)A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 18 to a human patient.

Claim 27. (Currently Amended)A sustained release oral dosage form comprising:

(a) a bilayer core comprising:

(i) a drug layer comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof; and

(ii) a displacement layer comprising an osmopolymer; and

(b) a semipermeable wall comprising a hydrophobic material selected from the group consisting of a cellulosic polymer, an acrylic polymer and a combination thereof surrounding the bilayer core having a passageway disposed therein for the release of said hydrocodone or pharmaceutically acceptable salt thereof; said dosage form providing a C_{24}/C_{max} ratio of 0.55 to about 0.85; and said dosage form providing a therapeutic effect for at least about 24 hours after oral administration to a human patient.

Claim 28. (Original)The dosage form of claim 27, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 29. (Original)The dosage form of claim 27, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 30. (Original)The dosage form of claim 27, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 31. (Original)The dosage form of claim 27, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 32. (Original)The dosage form of claim 27, wherein said administration is first administration.

Claim 33. (Original)The dosage form of claim 27, wherein said administration is steady state administration.

Claim 34. (Original)The dosage form of claim 27, which provides a dissolution release rate in-vitro of the hydrocodone or salt thereof when measured by the USP Basket Method at 100 rpm in 700 ml Simulated Gastric Fluid (SGF) at 37° C for 1 hour and thereafter switching to 900 ml with Phosphate Buffer to a pH of 7.5 at 37° C, of at least 20% by weight hydrocodone or salt thereof released at 4 hrs, from about 20% to about 65% by weight hydrocodone or salt thereof released at 8 hrs, from about 45% to about 85% by weight hydrocodone or salt thereof released at 12 hrs, and at least 80% by weight hydrocodone or salt thereof released at 24 hours.

Claim 35. (Original)The dosage form of claim 27, wherein said ratio is provided to a population of patients.

Claim 36. (Original)A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 27 to a human patient.

Claim 37. (Currently Amended) A sustained release oral dosage form comprising:

(a) a bilayer core comprising:

i) a drug layer comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof; and

(ii) a displacement layer comprising an osmopolymer; and

(b) a semipermeable wall comprising a hydrophobic material selected from the group consisting of a cellulosic polymer, an acrylic polymer and a combination thereof surrounding the bilayer core having a passageway disposed therein for the release of said hydrocodone or pharmaceutically acceptable salt thereof; said dosage form providing an in-vitro release rate, of hydrocodone or a pharmaceutically acceptable salt thereof, when measured by the USP Basket Method at 100 rpm in 900 ml aqueous buffer at a pH of between 1.6 and 7.2 at 37° C of from 0% to about 35% at 1 hour, from about 10% to about 70% at 4 hours, from about 20% to about 75% at 8 hours, from about 30% to about 80% at 12 hours, from about 40% to about 90% at 18 hours, and greater than about 60% at 24 hours; the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopoeia XXII (1990) at 100 rpm in 900 ml aqueous buffer, is no greater than 10%.

Claim 38. (Original)A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 37 to a human patient.